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Isolation and characterization of a cDNA encoding the KS1/4 epithelial carcinoma marker.

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The mAb KS1/4 recognizes a novel cell surface glycoprotein on a variety of epithelial carcinomas which may be a useful target Ag for antibody-directed diagnostic and therapeutic approaches. Here we report the isolation and characterization of a full length cDNA clone coding for the KS1/4 Ag, as well as, physical and biochemical studies on the antigen derived from an adenocarcinoma of the lung cell line. Affinity purification of the KS1/4 Ag reveals three glycosylated species by NaDodSO4 PAGE with molecular weights of 42, 40, and 35 kDa. The 42- and 40-kDa species are similar at the protein level, differing by their degree of glycosylation, and the 35-kDa protein results from a dibasic proteolytic cleavage of the larger m.w. species. Although both the 42- and 40-kDa forms are found on the cell surface, the 40-kDa protein appears to be the predominant species. A cDNA clone containing the complete KS1/4 coding sequence and the 5'- and 3'-non-translated regions was isolated from a library constructed from the human adenocarcinoma of the lung derived cell line, UCLA-P3. The cDNA clone contains an open reading frame of 314 amino acids which includes a putative signal sequence of 23 amino acids. Northern blot analysis shows a single RNA species of 1.5-kb. Sequence analysis of the 5' and 3' noncoding regions of the KS1/4 cDNA revealed homologies to known proto-oncogenes and inflammatory mediators.

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TUMOR-ASSOCIATED CALCIUM SIGNAL TRANSDUCER 1; TACSTD1

Alternative titles; symbols

ANTIGEN DEFINED BY MONOCLONAL ANTIBODY AUAI; MIC18
MEMBRANE COMPONENT, CHROMOSOME 4, SURFACE MARKER 1; M4S1
GASTROINTESTINAL TUMOR-ASSOCIATED ANTIGEN 2, 35-KD GLYCOPROTEIN GA733-2
EPITHELIAL CELLULAR ADHESION MOLECULE; EPCAM

Gene map locus 2p21

TEXT

CLONING

Spurr et al. (1986) characterized a human cell surface antigen that is defined by the monoclonal antibody AUAI. The gene product was expressed only on epithelial cells. The AUAI antibody detected a single 35-kD protein.

Szala et al. (1990) cloned the cDNA for GA733-2 from an expression colorectal carcinoma cell cDNA library transfected into COS cells and immunoselected with the GA733 monoclonal antibody. The predicted 314-residue protein is processed to the mature antigen of 232 amino acids. The glycosylated protein is predominantly 40 kD, although other species are observed. The same cDNA was identified independently by Strnad et al. (1989) from the lung adenocarcinoma cell line UCLA-P3 and designated KSA. Likewise, Perez and Walker (1989) obtained the identical cDNA, which they designated KS1/4 antigen. GA733-2 is about 49% similar to GA733-1 (137290). Both GA733 antigens have similar hydropathy plots, which include 2 hydrophobic regions. A domain at the amino end is predictive of signal peptides, while the hydrophobic domain at the carboxyl end is most likely a membrane spanning sequence. Northern blot analysis demonstrated a 1.45- to 1.5-kb transcript in cell lines derived from colorectal and pancreatic carcinomas. The mRNA was also detected in normal colon and in lung and colon adenocarcinoma lines.

GENE FUNCTION

Using flow cytometry to screen cell lines with a LAIR1 (602992) fusion protein, Meyaard et al. (2001) identified a LAIR1 ligand on colon carcinoma cell lines. By expression cloning from a colon carcinoma cDNA library, they showed that the LAIR1 ligand is identical to EPCAM. EPCAM also binds LAIR2 (602993), which is 84% homologous to LAIR1 in its Ig domain. Mutation analysis determined that EPCAM interacts with the LAIRs through its first EGF-like repeat. Flow cytometry and immunohistochemical analysis demonstrated LAIR1 expression in intestinal intraepithelial cells, in close proximity to cells expressing EPCAM. Meyaard et al. (2001) proposed that EPCAM, through its interaction with the LAIR1 inhibitory receptor, is involved in preventing excessive inflammatory responses in regions, such as intestine, with high antigen exposure.

GENE STRUCTURE

Linnenbach et al. (1993) showed that the gene encoding GA733-2 (M4S1) contains 9 exons. From studies of the GA733-2 genomic sequence and comparison of the promoter regions of both GA733-2 and GA733-1 genes, the authors concluded that GA733-1 was formed by the retrotransposition of the 9-exon GA733-2 gene via an mRNA intermediate.

MAPPING

Spurr et al. (1986) mapped the MIC18 gene to human chromosome 2 by analysis of human-mouse somatic cell hybrids. By PCR analysis, Durbin et al. (1990) confirmed the mapping of MIC18 to chromosome 2. Linnenbach et al. (1993) localized the GA733-2 gene to 4q by analysis of human/rodent somatic cell hybrids. Calabrese et al. (2001) mapped the TACSTD1 gene to 2p21 by fluorescence in situ hybridization.

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WEST

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Q2	Q1 and (ercc4 or xpf)	USPT	ASSIGNEE	ADJ	YES
Q3	Q1 and excision repair protein	USPT	ASSIGNEE	ADJ	YES
Q4	ercc4	USPT	ASSIGNEE	ADJ	YES
Q5	ga733-2 or ks1/4	USPT,PGPB,JPAB,EPAB	ASSIGNEE	ADJ	YES
Q6	Q5 and Q1	USPT,PGPB,JPAB,EPAB	ASSIGNEE	ADJ	YES

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